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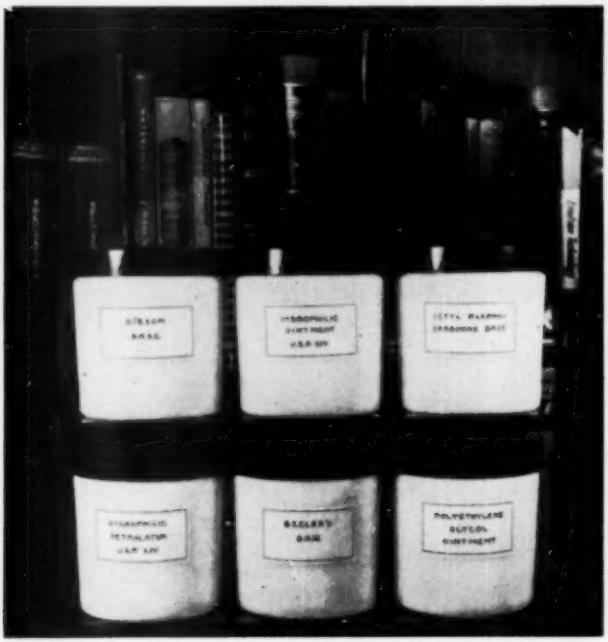

See Article on Modern Ointment Bases, page 208.

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EDITORIAL

PHYSICIAN-OWNED PHARMACIES

THIS subject has aroused considerable concern in certain areas of the country and it is likely to receive more and more attention in the future. Pharmacies which are owned wholly or in part by a physician or a group of physicians are indeed somewhat questionable from the standpoint of medical ethics and a number of medical groups are on record as opposing such practices. The point has been made, and quite properly so, that when the physician profits from the sale of medication he is tempted to be influenced in his prescribing by the economic factors involved. An obsolete drug, which he knows is heavily inventoried, may be prescribed until it is gone rather than a superior product. An expensive drug, on which the profit is high, may be prescribed when a less costly drug is equally efficient. The independent pharmacist, on the other hand, must take a loss on an obsolete drug and he is in no position to require the use of costly drugs on prescription. Physician-owned pharmacies quite understandably present the independent pharmacist with unfair competition since patients are loathe to risk the physician's displeasure by taking the prescription elsewhere when a certain pharmacy is directed or even suggested by implication. In some instances the physician employs a nomenclature or a code number known only to the pharmacy which he specifies. This is a nefarious scheme if there ever was one.

A similar practice, even more common and much more hazardous, is for the physician to house his own pharmacy and have a nurse or even a person with less training compound and dispense medication. The evils and excesses encompassed in this seemingly accepted practice, were they fully known, would surely shake public confidence in the supposed infallibility of the physician. The things that happen are well concealed but they are atrocious as every honest physician knows only too well.

Pharmacists, generally, know about these things but, unfortunately, when they speak out against them they are accused of being

motivated solely by the factor of lost profits. Too often, we fear, the profit motive *is* in the minds of pharmacists when they frame resolutions or petition medical societies to correct these evils. Some pharmaceutical groups seem to feel that legislation is the answer to this problem. They propose that physicians be restrained by law from owning pharmacies. Such a viewpoint is both naïve and unrealistic. Unless the time comes that we can restrict pharmacy ownership to pharmacists no such restrictive class legislation against physicians will be held constitutional. If a bricklayer can own a pharmacy surely no state or federal legislative body will prevent a physician from doing so. The legislative influence of physicians should not be taken lightly and it is very doubtful whether pharmacy could hope to better the medical profession in a legislative battle.

The suggestion has been made that pharmacists who accept employment in physician-owned pharmacies be adjudged guilty of professional misconduct and barred from membership in state and national pharmaceutical organizations. To do this without similar action against those pharmacists known to be a party to malpractices in other directions would be inconsistent, difficult if not impossible to implement, and a futile gesture.

What then is the answer to this growing problem? It is simple, so much so that it probably will be ignored just as are so many logical and simple answers to human and social problems. When we as pharmacists prove to the public at large, including the medical profession, that we are motivated primarily by a sincere concern for public welfare then this dereliction by the medical profession will cease. There is no force which is the equal of moral force but it is today rarely used. We have today on the American scene a sorry example of the results of name calling and pressure tactics, with group fighting group with the din and the turmoil becoming almost incessant. If the few remaining stabilizing influences of society: the professions, the clergy and our educators succumb to this same policy then we shall soon become a nation of selfish groups screaming hatred for everyone else until we all are swallowed up by our own greed.

We in pharmacy have much to do to put our own house in order. When it is done we shall not need fear the results of the misconduct of others. It is our own weakness which makes us both vulnerable and afraid.

L. F. Tice

MODERN CONCEPTS FOR THE PREPARATION OF OINTMENT BASES *

By Elsa Ehrenstein **

DURING the last few years the concept of an ointment base has undergone considerable change, as evidenced by the U. S. P. XIII and XIV which give official recognition to some of these changes. The proper understanding of the underlying principles in selecting the ointment-vehicle type presents a challenge to the pharmacist's professional knowledge. Not only is it the duty of the pharmacist to obtain a uniform and a smooth distribution of the medication throughout the ointment base and to see to it that such a preparation is stable and permanent, but he also should keep in mind the therapeutic effects that should be produced by an ointment.

It is true that the physician is charged with the primary responsibility for the proper dosage of the medication and also with the selection of the appropriate ointment base to obtain the desired therapeutic effect. The physical state of the ointment vehicle will be shown to have an important bearing on the function of an ointment used in dermatologic therapy.

An ideal ointment base should possess the following characteristics:

1. Affinity for the skin; i.e.: it should be miscible with both aqueous and oily secretions of the skin and it should meet the conditions of the skin, particularly the pH. Thus, its pH should be 5.5—7.0;
2. Stability;
3. Permanency;
4. Pliability or smoothness;
5. Non-irritating: non-sensitizing as such and in combination with other ingredients;
6. Inertness against chemicals to be incorporated;
7. Ability to absorb water or other liquid preparations;
8. Ability to release easily its incorporated medication.

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* Lecture given at a Seminar before the Montgomery County Pharmaceutical Association, April 25, 1950, Philadelphia, Pa.

** Assistant Professor in Pharmacy, Philadelphia College of Pharmacy and Science.

There is no single ointment base which possesses all these characteristics. We must be satisfied with preparations where at least some of these desirable attributes are obtained, and in each specific case we have to take into consideration for what purpose the ointment is to be used. Therefore, the division of ointments into 4 groups for therapeutic effect becomes very important. What ointment bases will, in each instance, produce these effects? See Table I for classification.

1. *The Protective Ointments or Epidermic Ointments*

For this type the petrolatum base ointment lends itself very well. Petrolatum is a mixture of hydrocarbons, with no affinity for water. In this fact, however, lies its disadvantage for use in those types of ointment intended for absorption or penetration. It absorbs water only to a very small extent (about 5%). When applied to the skin, it serves only as a protective covering, but even then it prevents natural perspiration, since it does not mix with aqueous exudations of the skin. However, it is a very stable, inert ointment base, easily applied, and where only a protective covering is desired, it is a base of choice. It is not prone to decomposition, will not become oxidized, it is cheap, can be purified, and lends itself well for incorporation. However, an antagonism exists between the petrolatum or oil phase, and the water phase, which is represented by the aqueous exudations of the skin, its moist surface, or the aqueous surface of a wound. Therefore, the ointment is prevented from coming in intimate contact with these tissues. The presence of an emulsifying agent or a wetting agent in an ointment base exerts a profound effect on the activity of the ointment by lowering the interfacial tension and permitting a free exchange between the tissues and the ointment. As a direct result, penetration and drug release are markedly increased and removal of the ointment is simplified. By the addition of an emulsifying agent, the petrolatum base can be made either hydrophilic (water absorbing) or water washable.

Emulsion Type Ointment Bases

These may be divided into the oil in water type emulsion and water in oil type emulsion.

Emulsion bases, as the term implies, are vehicles having two phases. An emulsifying agent is employed to reduce the interfacial tension and thus stabilize the emulsion.

TABLE I

Ointment Bases

Classification Based on Their Physical Characteristics

1. Protective Ointments	2. Emulsion type bases (Absorption type, w/o type)	3. Emulsion type bases (water washable)	4. Water soluble bases; greaseless ointment bases
Hydrocarbon Bases (no affinity for water)	a. *Absorption bases forming w/o emulsions upon the addition of water.*	*o/w Emulsion type*	1. Polyethylene Glycol Ointment U. S. P. XIV
Petrolatum	1. * Hydrophilic Petrolatum U. S. P. XIV	1. ** Hydrophilic Ointment U. S. P. XIV	2. Ointment base containing 3 polyethylene glycols
* White Ointment	2. Wool Fat U. S. P. XIV	2. Beeler's Base	3. Pectin Paste, N. F. IX
* Yellow Ointment	3. Aquabase	3. Cetyl Alcohol-Carbowax Base and Water	4. Thin Pectin Paste N.F. IX
	4. Aquaphor	4. Gibson Base	5. Bentonite Base Ointments
	b. *w/o type emulsion bases*	5. Glyceryl Monostearate Base	
	1. Hydrous Wool Fat U. S. P. XIV	6. Span and Tween Base containing Stearic Acid	
	2. Rose Water Ointment U. S. P. XIV	7. Hydroxystearin Sulfate Ointment	
	3. Petrolatum Rose Water Ointment U. S. P. XIV		

* Formulas for these ointments have been changed in the U. S. P. XIV. Wool Fat has been deleted from all U. S. P. formulas, since it is claimed to have marked sensitizing properties. In the hydrophilic petrolatum the amount of cholesterol has been increased from 10 Gm. to 30 Gm. for 1000 Gm. of finished ointment.

** Hydrophilic ointment U. S. P. XIV has only one minor change: Glycerin is replaced by propylene glycol.

2. Water in Oil Emulsion Bases

The first group of these penetration ointments are the W/O type ointment bases, which differ considerably from the O/W type base. They are much more greasy. Some of these bases are themselves anhydrous but are capable of taking up a large amount of water; this fact is the outstanding difference between the O/W and W/O type base. The pharmacist is very often called upon to incorporate relatively large amounts of an aqueous preparation such as Coal Tar Solution, Burow's Solution or Lead Subacetate Solution into an ointment base. In such a case he has to resort to an ointment base which is able to take up large quantities of liquid.

The official representative of this group is Hydrophilic Petrolatum. See Table I. It may also be called an anhydrous ointment base, since it does not contain any water. It is official in the present U. S. P. and will be continued in the U. S. P. XIV. The term hydrophilic designates water-loving, thus indicating that this base is capable of taking up a large amount of water. The term "Absorption Base" refers to this characteristic. The formula in the U. S. P. XIV differs from the previous formula in the fact that wool fat is omitted. Cholesterol is an agent which produces hydrophilic properties. When aqueous preparations are added to this ointment base a W/O emulsion is formed. These W/O emulsions have good penetrating properties but they are not easily washed off, since oil is the external phase. Wool Fat and Hydrous Wool Fat show these same water-absorbing properties. It is interesting to note that, although Wool Fat and Hydrous Wool Fat will still be official in the U. S. P. XIV, these two ingredients have been deleted from all U. S. P. ointment bases and medicated ointments. (White ointment, yellow ointment, zinc oxide ointment, etc.) Many dermatologists claim that wool fat is a marked sensitizing agent, and they complain bitterly that the general practitioner does not recognize this condition. The dermatologists see many patients with skin conditions caused by allergic reactions to wool fat. It might be well for the pharmacist to keep this in mind, since wool fat is such a very popular ointment ingredient.

An ointment base similar to the rather well-known Aquaphor is the so-called Aquabase, whose formula is listed on Table II.

TABLE II

FORMULA FOR AN ABSORPTION TYPE BASE
FORMING W/O EMULSION UPON THE ADDITION OF WATER

Aquabase:

Cholesterol	3.0 Gm.
Cottonseed Oil	3.0 Gm.
White Petrolatum to make	100.0 Gm.

Heat the white petrolatum and cottonseed oil to 145°C. Remove from heat, add the cholesterol and stir until almost congealed. Pour into jars.

3. *Oil in Water Emulsion Bases*

Emulsifying agents which favor the production of oil-in-water emulsions are alkali soaps, triethanolamine soaps, sulfated alcohols, alkyl aryl sulfonates, etc.

A water washable ointment base of the O/W type, Hydrophilic Ointment, will be official in the U. S. P. XIV with a minor change from the formula in the U. S. P. XIII. Propylene glycol is the humectant rather than glycerin, because the latter prevents the softening of the ointment upon incorporation of salicylates. This ointment lends itself very well for penetration. It contains a rather large amount of water (37%), an excellent surface-active agent (sodium lauryl sulfate) which makes application and removal of the ointment quite easy, propylene glycol (U. S. P. XIV), acting as humectant; stearyl alcohol which increases the consistency of the ointment; methylparaben and propylparaben are preservatives and white petrolatum is the base. This official ointment is a typical representative of water washable ointment bases. It is an O/W emulsion, mixes readily with the oily and aqueous secretions of the skin and releases the medication very easily. It is a typical example of a modern ointment vehicle, a fine smooth cream, and is favorably accepted by the patient. In all such ointment bases which consist of a water and an oil phase, the key to obtaining a uniform smooth mixture lies in the fact that the water and oil phase must be heated separately to the same temperature (about 75°C.), then mixed together and stirred vigorously until cool. A mechanical stirrer or a homogenizer (previously warmed with hot water) are pieces of equipment which speed up the preparation of a

good ointment base and these should be available in any well-conducted prescription store.

Since there is a large amount of water present in this ointment it must be protected from water loss by evaporation. It is suggested that medication be incorporated into this base in a mortar, rather than on a tile, thus reducing the surface area of base exposed to the air. After the ointment is made, it should be stored tightly to prevent water loss. If water is lost the finished ointment will have a dry, grainy appearance, the medication will be in a much greater concentration than was originally intended by the prescriber and this may give rise to serious problems. The rate of release of the active principle from the base plays a very important role in these water washable ointment bases. Penetration of the medicinal substance is easily accomplished and eventually this substance may be absorbed into the circulatory system. Toxic effects can thus be produced and consultation with the physician or dermatologist may be needed to safeguard the patient against untoward effects when these water washable bases are used. For instance, Coal Tar Ointment should not be dispensed in a hydrophilic base, since this would help the carcinogenic substances known to be present to penetrate the skin more readily. Experiments with sulfadiazine in different ointment bases have shown that a much greater penetration is obtained in a hydrophilic base than in white ointment. However, the fineness of the powder also plays a very great role. Microcrystalline powders should be used wherever possible, since they diffuse much more readily.

Boric Acid should not be incorporated into a water washable base, since it is a well known fact that it can cause toxic effects. Chrysarobin must not be incorporated into a hydrophilic base. The Pharmacopeia only provides the several bases and allows physicians to try their own combinations.

These facts show clearly that medication is much more readily released from hydrophilic ointments, that the amount of medication generally should be reduced, and that an official ointment made with a petrolatum base cannot arbitrarily be prepared with a water washable base.

There are many more formulas of the O/W type emulsion published and a list is included for general information. See Table III.

Bases of this group present products of cosmetic-like appearance and mark a great step forward in topical application; they simulate the vanishing creams.

TABLE III

FORMULAS FOR OINTMENTS OF THE O/W EMULSION TYPE (WATER WASHABLE)

1. *Hydrophilic Ointment U. S. P. XIV*

This formula differs from U. S. P. XIII only in the fact that propylene glycol is employed instead of glycerin.

2. *Beeler's Base*

Cetyl Alcohol	15.0 Gm.
White Wax	1.0 Gm.
Propylene Glycol	10.0 Gm.
Sodium Lauryl Sulfate	2.0 Gm.
Water	72.0 Gm.

Melt the cetyl alcohol and white wax in the propylene glycol and heat to 65°C. Dissolve the sodium lauryl sulfate in the water, heating to 65°C. Add the oil phase to the water phase, constantly stirring, continue heating for about 10 minutes. Then stir until congealed.

3. *Cetyl Alcohol—Carbowax Base with Water*

Cetyl Alcohol	25.0 Gm.
Carbowax 1500	25.0 Gm.
Sodium Lauryl Sulfate	1.0 Gm.
Water	49.0 cc.

Heat cetyl alcohol and Carbowax on water bath to about 70°C., dissolve sodium lauryl sulfate in water, heat to same temperature, mix the two phases, stir until congealed. Mechanical stirrer is advisable only if slow speed is used, otherwise separation occurs.

4. *Gibson Base*

Sodium Lauryl Sulfate	1.0 Gm.
Cetyl Alcohol	16.0 Gm.
White Petrolatum	40.0 Gm.
Water	43.0 Gm.

Dissolve the sodium lauryl sulfate in the water and heat the solution to 70°C. Melt cetyl alcohol and white petrolatum, on water bath to a temperature of 70°C., and add to the aqueous phase using a mechanical stirrer. Stir until cooled.

TABLE III (Continued)

5. *Glyceryl Monostearate Base*

Glyceryl Monostearate	12.0 Gm.
Light Liquid Petrolatum	20.0 Gm.
White Petrolatum	20.0 Gm.
Water	48.0 Gm.

The components are mixed and melted at a temperature at 70°C., stir until emulsion forms and continue stirring until congealed.

6. *Span and Tween Base Containing Stearic Acid*

a). Stearic Acid	12.0 Gm.
Span 60	10.0 Gm.
Tween 60	6.0 Gm.
Water	72.0 cc.

Warm oil phase and water phase separately to 95°C. Pour oil phase into water phase gradually and stir until cool. A homogenizer proves very useful, but must be pre-warmed.

b). Same formula as above, only 10% of white wax is used, leaving only 62 cc. of water. This ointment base is somewhat firmer.

c). Same formula as 6a, only 10% of ozokerite is used, leaving only 62 cc. of water.

This ointment base is also slightly firmer, and has a very fine texture with a slightly yellowish tinge.

d). Same formula as 6a, only 10% of glycerin is used, leaving 62% of water.

e). Again same formula as 6a, replacing 10 cc. of water with propylene glycol.

These formulas are slightly modified from a formula list by the Atlas Powder Company in "Drug and Cosmetic Emulsions."

These formulas lend themselves to various changes, such as substituting stearyl alcohol for stearic acid, or a mixture of stearyl alcohol and cetyl alcohol in a suggested proportion of 87.5% stearyl alcohol and 12.5% cetyl alcohol.

7. *Hydroxystearin Sulfate Ointment*

Hydroxystearin sulfate	33%
Petrolatum	50%
Glyceryl monostearate	17%

Melt the ingredients together on a water bath and stir until congealed. The emulsions formed with hydroxystearin sulfate are of the oil in water type.

General Comments on O/W Emulsion Type Bases:

See Table III.

The wetting agent, i.e. sodium lauryl sulfate, should be maintained at a minimum, usually not more than 1%, in dermatologic preparations since it is apt to make the preparations very drying.

1. *Hydrophilic Ointment:*

The change from glycerin to propylene glycol in hydrophilic ointment was made because hydrophilic ointment very often softened when it was levigated. Propylene glycol overcomes this objectionable factor.

2. *Beeler's Base:* This smooth ointment feels slightly greasy but washes off rather easily. It is compatible with most dermatological ingredients. The pH is approximately 7. It is stable at temperatures between 0° to 50°C.; autoclaving, however, causes separation. It is important to maintain the temperature at 65°C. for about 10 minutes after emulsification has taken place. It must be kept in mind that these O/W emulsion type bases must be protected from water loss, otherwise they will crumble and dry out. This base should not be used for the eye or on mucous surfaces (1).

3. *Cetyl Alcohol—Carbowax Base containing water:* This again is a very smooth base but slightly greasy.

Follow procedure. Hand mixing produces a very uniform product. Mechanical stirrer at a rather high speed causes separation, and ointment can be reclaimed only by reheating the mixture and subsequently stirring by hand. Slow speed will probably prevent separation.

4. *Gibson Base:* This is a smooth, slightly greasy base but it washes off easily.

Sodium lauryl sulfate is the surface active agent employed in 1% strength. A smooth cream-like base is produced (2). Slow speed mechanical stirrer can be employed.

5. *Glyceryl Monostearate Base:* This is a smooth base which washes off easily.

This base is easily emulsified, but appears to be lumpy at first; upon standing it makes a very smooth product. Very little water is lost from this base on standing (2).

6. *Span and Tween Base containing Stearic Acid:*

This ointment was used quite extensively for experimental work and it facilitates the incorporation of many dermatologic ingredients. If it seems too soft the formula can be varied by adding wax or ozokerite in necessary amounts.

All these bases show a tendency toward forming a slightly granular product on standing; however, these grains can be rubbed smooth very easily. The bases containing waxes are stiffer, the white wax base forming a smooth product, the one with ozokerite being slightly more granular.

The base containing glycerin does not have any sheen, looks slightly dry, but upon levigation returns to smooth consistency. The base containing propylene glycol is very smooth and does not show any granular appearance. It seems that the Spans and Tweens lend themselves very well as emulsifying agents.

There are many more formulas available in the literature and also several ointment bases are placed on the market labeled as being water washable.

It is claimed that reduction of water loss can be obtained by adding combinations of cholesterol and cholesteryl stearate, cetyl alcohol and cetyl-12 hydroxystearate (*2*).

If these preparations are to be stored, preservatives must be added. Methylparaben and propylparaben are suggested.

4. *Water Soluble Ointment Bases*

This is the fourth and last group. With the advent of synthetic compounds the formulation of ointment bases has undergone major changes. The most important ingredients making up these water soluble bases are the "Carbowaxes" which are chemically polyethylene glycols of the general formula $HOCH_2(CH_2OCH_2)xCH_2OH$. The outstanding feature of these Carbowaxes is their chemical inertness and their solubility in water. The Carbowaxes provide a preparation which looks and feels like petrolatum, but yet it is water soluble. It helps absorption and has the feel of an ointment. It gives up water, solutions and chemicals to tissue better than the official Hydrophilic Ointment.

The Carbowaxes have a wide range in molecular weight. Those with molecular weights ranging from 200-700 are liquids; those above 1000 are wax-like solids. Prior to the development of these higher polyethylene glycols, a compound having a combination of both unctu-

ous and water soluble properties was not available. Consequently, attempts to make water-soluble ointment-like preparations were concerned principally with emulsions and suspensions of oil in water which were just discussed. With the development of these compounds it is now possible to control the consistency of an ointment base by blending these compounds with members of different molecular weights. Thus, the U. S. P. XIV will recognize an ointment base of equal parts of polyethylene glycol 400 and 4000 producing a smooth inert ointment base. By using different members of the Carbowax series and different proportions almost any desirable consistency can be obtained. For instance, by mixing Carbowax 1500 and 4000 with propylene glycol or polyethylene glycol 400, ointments of any desired consistency may be prepared. (Table IV.) These bases lend themselves very well for extemporaneous preparation. The addition of some organic acids and phenol tend to soften the final product. 5% cetyl alcohol increases the stability of these ointments. Since the Carbowaxes are actually soluble in water not more than 3 per cent of water can be incorporated into these Carbowax bases. They are, therefore, anhydrous bases.

Emulsion type bases can be prepared from them by adding stearyl alcohol, glycerin and an emulsifying agent. (Similar to the Cetyl Alcohol-Carbowax base under the O/W type bases.) The emulsifying agent can be Span 40 or sodium lauryl sulfate.

Higher polyethylene glycols do not hydrolyze or deteriorate, and they will not support mold growth.

Of primary interest to practicing pharmacists is Carbowax compound 1500, which is particularly suited as a base or vehicle for drug or cosmetic preparations. It is said to give the creams superior softening and skin-smoothing properties without undesirable moist or "tacky" feeling on the skin. Its use is also suggested as a component of shaving creams, pomades, and hair dressings (3). A wide field of experimental work can still be carried out, and our professional journals publish quite a variety of ointment formulas.

The official polyethylene glycol ointment of the U. S. P. XIV is a homogeneous, white, semisolid base similar to petrolatum in consistency and liquefies at 52°C. It is completely water soluble and non-staining to bed linens and clothing. Tests show that it remains relatively unchanged upon storage at room temperature for indefinite periods and can, therefore, be recommended as a stock vehicle.

TABLE IV

Formulas for Water Soluble Bases

(Also Called Greaseless Ointment Bases)

1.) *Polyethylene Glycol Ointment, U. S. P. XIV*

Carbowax 4000	50 Gm.
Polyethylene Glycol 400	50 Gm.

Heat the ingredients together on a water bath until melted, stir until congealed.

2.) *Ointment Base Containing 3 Polyethylene Glycols*

Carbowax 4000	40 Gm.
Carbowax 1500	30 Gm.
Polyethylene Glycol 400	30 Gm.

Melt the ingredients together on a water bath, stir until congealed.

3.) *Greaseless Base With Bentonite*

Glyceryl monostearate	10 Gm.
Glycerin	25 Gm.
Bentonite	2 Gm.
Distilled water, sufficient to make	100 Gm.

Sprinkle the bentonite upon 50 cc. of distilled water and after it is thoroughly wetted, stir until a uniform magma results. Melt the glyceryl monostearate in the glycerin on a water bath and add it to the magma warmed to the same temperature, and then add enough distilled water to make the product weigh 100 Gm. Stir until cool. Use a homogenizer.

Lower concentrations of antiseptic agents in this type of base are as effective as much higher concentrations of the same agent in oleaginous bases. It is compatible with practically all medicinal agents used in dermatological practice. Salicylic acid, however, in concentrations larger than 3% tends to soften the ointment and it is suggested in such cases that 5% of cetyl alcohol be incorporated in the base. Small amounts of cetyl alcohol or stearyl alcohol tend to inhibit the solubilizing effect of water, alcohol, or the salicylates on polyethylene glycol and with such addition up to 20% of water can

be incorporated. When large amounts of powders are to be incorporated, it is best to use a small amount of propylene glycol or glycerin as levigating agent, otherwise the resulting ointment would be too firm for smooth application.

Carbowax can also be used for a hydrous base. A typical formula is:

Carbowax 4000	50 Gm.
Polyethylene glycol 400	40 Gm.
Span 40	1 Gm.
Water	9 Gm.

Again the ratio between Carbowax 4000 and polyethylene glycol 400 can be changed in order to obtain firmer or softer ointments. Span 40 has a low index of sensitization, because it is non-ionic. It can be replaced by sodium lauryl sulfate, or Aerosol OT, but these latter agents may prove to be more irritating.

All the Carbowax bases do not differ from the oleaginous preparations in their method of incorporation with medicinal agents. Ointments may be prepared either on a slab or in a mortar. Coal Tar, Ichthammol and Peruvian balsam do not require any special treatment.

In concluding the discussion of these water soluble Carbowax bases, it may be said that only time will prove the value of these bases. From the standpoint of acceptability by the patient they most certainly present a great advantage over the oleaginous vehicles.

We also can include under the heading "water soluble bases" Pectin Paste and Thin Pectin Paste of the National Formulary, and ointment bases containing bentonite; truly "greaseless" ointment bases.

The pectin pastes find their application for the treatment of bed sores and ulcers; their value depends on keeping the surface moist and in providing a salt medium (Ringer's solution) in which the survival and multiplication of cells appear to be enhanced. Because of the stability of pectin in acid media, its efficiency as an emulsifying and gelling agent, and its ability to bind large amounts of water in a semi-solid preparation, pectin is finding increasing use in the preparation of pharmaceutical and cosmetic products. It is decomposed in alkaline media. In order to prevent lumping of the pectin, it is always advisable to first moisten is with a small amount of glycerin before adding water.

The bentonite bases have attained more and more importance within the last few months (4). Bentonite, except for slight alkalinity, is practically inert chemically; it is odorless and it can be sterilized by heat prior to use. Most investigations along these lines are still of an exploratory nature, but these may eventually lead to some official formulas.

Bentonite Gel

Ointments with bentonite gel as a base, when spread very thinly on the face or hands are invisible and leave the skin surface smooth as if recently powdered, not greasy or sticky. The addition of glycerin or propylene glycol slows the drying out of the gel either in a jar or on the skin.

Bentonite Gel is a suitable base for water soluble drugs and for sulfonamides, fatty acids, salicylic acid and other substances which may be dissolved in propylene glycol or other suitable solvent before adding to the prepared base. Sulfur, ammoniated mercury, zinc oxide and other insoluble powders are readily incorporated in these bases.

Formula:

Bentonite	20 Gm.
Talc	10 Gm.
Water	55 cc.

Mix the bentonite with the talc and add slowly to the water with vigorous stirring. Soak overnight, rub smooth and add:

Glycerin	5 cc.
Liquid petrolatum	5 cc.
White petrolatum	5 Gm.

Melt the petrolatum in the liquid petrolatum, before adding to the gel (5).

In conclusion, it may be said that there is still very much work to be done on these newer ointment bases. The pharmacist is confronted with a definite challenge and can easily work out some formulas. Some firms have placed ointment bases on the market, such as Neo-Base, Uni-Base, Multi-Base, Jelene. A formula for these bases is not given, but they seem to be compatible with most dermatological products.

It is in such work as this that the pharmacist can show his desire to cooperate with the physician and be truly an adviser where pharmaceutical problems are involved.

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THE SPIRIT OF INTEGRATED HEALTH SCIENCES *

By Samuel P. Wetherill **

MR. President, Honored Guests, Distinguished Faculty, Loyal Students and Friends of the Philadelphia College of Pharmacy and Science:

In anticipation of this historic event, I have been bedevilled by the truly difficult choice between confining my remarks to a congratulatory spirit, on the one hand, or, on the other hand, to making an attempt to define the broader challenge which confronts us in these preëminently scientific times. There is not time to discuss both adequately, yet neither alone will suffice. Therefore, we must accept a compromise, which will of course be inadequate from either point of view.

To begin with, no one who knows the recent history of this college and the evolution of its spirit, its academic standing and the extension and improvement of its facilities, could possibly refrain from exclamations of joy and satisfaction at the progress which has been made, on not one but on all of these scores, under the inspired and inspiring leadership of our distinguished and beloved president, Dr. Ivor Griffith.

As Chairman of the Board of Trustees throughout the period of his incumbency, I have been, and am, in a rare position to make a dispassionate and qualified appraisal of this progress and I hereby pronounce, with great emphasis and sincere conviction, that the epoch brought to a focus by today's events, has been the most significant one in the whole life of this institution. Administrative order and genuine teamwork have been attained and the best traditions of the college lived up to and improved upon.

Thanks to the zeal just mentioned and to the generosity of our friends, we are now equipped, united and inspired to render our best service to the advancement of human health through leadership in teaching health sciences.

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* Delivered on the occasion of the dedication of new laboratories of Pharmacology, Pharmacy and Bacteriology at the Philadelphia College of Pharmacy & Sience, May 17, 1950.

** Chairman of the Board of Trustees, Philadelphia College of Pharmacy & Science.

Airplane View

Now—please hold your hats! Even our sights must now be raised. Let us turn to the great and growing challenge confronting all public health agencies. A number of us in the higher age brackets will do as my sagacious and recently demised friend did. He saw that most of us are zealously fishing, over the side of the ship, each trying for a good catch for his own basket—all too absorbed to heed a warning that if we don't man the pumps we'll go down together. "Then what good" he asked "will our baskets be?" He saw the problem and, like Louis XV, dodged it; by dying without waiting for the "deluge". If *we* don't, *who will* turn to the long range and growing problems in the field of public health, which are especially challenging to those who feel themselves potentially capable of helping in their solution.

Or, instead of turning to them, shall be turn away and share the blindness of those who will not see? If we do, we will have to shut our eyes to familiar sights that could disturb our sleep. Also, maybe blindness won't suffice to excuse evasion of responsibility. We may have to hold our noses or learn that "God's free air" is being sorely befouled and polluted in this, our great city of brotherly love, and in others no less. Shall we also stop our ears to deaden nerve shattering evidence that growing congestion, and its consequent traffic of bigger and better vehicles, threads its roaring way among dodging school children and their parents? Too often the ambulance siren will get through to our insensitive ears.

Even so, all this is not enough! Ever so slight a taste of chlorine in our drinking water, tea or coffee, will remind us of our filthy custom of looking up stream, toward inconsiderate neighbors, for our drinking water; while looking down stream toward our other neighbors, to whom we blithely dispatch our waste without so much as a fleeting prayer for their survival.

Is soil exhaustion clearly a problem for the farmer alone, in terms of quantity of yield and price of vegetables, and can we continue to tolerate fertilizing methods approved by Liebig, but frowned upon long ago by Pasteur? Can we expect to murder with chemicals and sprays and starve the soil micro-organisms whose operation and by-products we can prove are essential to healthy and abundant crops—in turn essential to healthy people?

Could we, if we would, fairly assess the cumulative effect upon our posterity—if not ourselves—of forest destruction, soil erosion and

lowering water tables? Maybe New York's recent dearth of water may sound a needed warning to those of us accustomed to take nature's bounty for granted while we jeopardize it for a more numerous posterity!

Vast as has been the scope and profundity of scientific progress in the treatment of disease and in the prevention of disease, new problems—which result chiefly from the rapid increase in population density—arise faster than solutions for the old ones are found.

The time appears to be at hand when the erstwhile code of ethics for scientific reliability and thoroughness, which has done so much to build the fame of the Philadelphia College of Pharmacy and Science, will no longer suffice in the fulfillment of our obligations, if not to our times, then certainly to our posterity.

People of all nationalities and of all parts of the earth, are confronted with the necessity to quarantine themselves from the negligence of others. An aeroplane from North Africa, if not properly fumigated, carries insects and diseases to another continent overnight. Unsanitary procedures and habits—like obsolete habits of thought and the ruthlessly selfish aims of a few—have in a twinkling, wreaked havoc over the face of the earth and threaten more of the same or worse.

Innumerable examples will come to mind of the extent to which we are dependent upon one another. We want products from Holland and Japan and Africa but we don't want Dutch elm borers, Japanese beetles or the African tsetse fly. Neither we nor Mexico want hoof and mouth disease in cattle herds but we rebel against the best known correction for this which seems to be the near extermination of our respective herds. The simplest scientific problems raise acute international issues. Science, our heralded savior of mankind, increasingly threatens his very survival.

As scientists, concerned with the health of present and future generations, how long can we tolerate the lowering of the water table and the consequent impairment of the quantity and quality of food and pasture? How long can we tolerate the heedless and revolting practice of converting our beautiful rivers and erstwhile pristine streams into filth carriers? What is the matter with our imaginations that they are callous to the spiritual devastation caused by putrid odors arising from our rivers; to the consciousness that we are drinking treated sewage; of the foul pollution of the air, which may be ap-

praised, for example, when the wind blows from Southeast Philadelphia over to the campus of our great sister institution, the University of Pennsylvania, and at times makes breathing in our own Clark Park an ordeal? Can this sort of thing be permitted to continue and run the costs of inadequate correctives cumulatively into far greater sums than would be the cost of research and determined development of alternate practices. We can keep our health, our happiness and our prosperity, if we only will. There are great spiritual values to be realized through the contributing of our independent but united spirit of dedication to the welfare that can ensue to our posterity. We can co-operatively restore and perpetuate the opportunity of joyful and self-respecting living which blessed the settlement, for example, of this, Penn's Holy Experiment.

My plea, Mr. President and Fellow Citizens, is that we recognize these problems and devote ourselves to their proper solution before they overwhelm us. Even if we, individually, see nothing we can do about them, let us at least awaken among ourselves and our neighbors, the will to win this battle for survival of our kind. I am not alone in loving people best of God's creatures! Collectively, let us devote ourselves to their progressive correction before it is too late. It's later now than we realize. If we do not feel degraded by the environment which seems to be everyone's business and yet no one's, then there must be something the matter with us and we must cure it. If we do feel degraded and do nothing about it, then we subject ourselves to further degradation. We cannot expect leadership in these directions from the masses of people who accept their environment as they accept the weather or as the cow accepts the passing train. The training in this college has been constantly to add to the element of scientific thoroughness and proficiency, the additional element of a high concern for public welfare.

At our high level of health and longevity and with each individual seeking to develop his own latent powers and life's opportunities to the utmost, there still must also be developed those who see in the solution of public welfare problems the highest satisfaction to their personal ambitions and the most promising opportunities for their individual successes. We must integrate the conclusions of all of our separate sciences into a thoroughly modern philosophy of group acceptance of responsibility for the solution of the overwhelming threats to our civilization, for which none but resourceful and profoundly

devoted scientists can hope to offer practical solutions. Cures for our diseases are not enough. Even prevention of many specific ills is not enough. Nothing will suffice but skillfully led and nobly inspired dedication to the welfare, and spiritual, as well as material, emancipation of our posterity. Specialized and well endowed research must be undertaken, in accord with comprehensively planned priority programs. A new marriage of realism and vision is needed now, lest soon the people perish!

What better date could be recorded for the co-operative acceptance of this challenge by this great college, with its improved human and physical resources and traditions, than *this* date—May 17, 1950, on which these laboratories are here dedicated; this date on which the soul and spirit of this old College of Pharmacy and the Health and Sciences now dedicates itself anew to the health, welfare and happiness of the interdependent teeming millions of the earth?

We are indeed laying the corner stone of the new era—Independent Interdependency!

ABSORPTION AND LIBERATION OF EPHEDRINE FROM ION EXCHANGE RESINS

By C. Lee Huyck *

ION exchange resins have been suggested as alkaloidal absorbents (1). Also they have been suggested as a possible new method for the assay of alkaloids as such and in galenical preparations. Jindra (2) has reported that Amberlite 1R-4B shows some promise in the assay of alkaloids. It has the advantages of rapidity, simplicity and the use of a small quantity of solvent. The purpose of this investigation was to test the efficacy of this method for the determination of ephedrine in alcoholic solutions.

Experimental.

The ion exchange resins used were Dowex 50 and Amberlite IRC 50. They were packed in 15 cm. calcium chloride tubes of 1.5 cm. internal diameter. A small pledget of cotton was placed in the bottom of the tube making the column about 7 cm. in height. To check the relative efficiencies of these two exchangers for the absorption of ephedrine, 20 cc. of a 1% solution of ephedrine in unneutralized alcohol was allowed to drip on the exchanger as fast as the tube would take it. (60 drops per minute.) The liquid that came through the column was assayed by the method given in the U. S. P. XIII for ephedrine in that an excess of n/10 HCl was added and the excess was titrated with n/10 NaOH using methyl red test solution as indicator. The exchanger was then washed with two 20 cc. portions of 95% unneutralized alcohol and each portion was assayed. The results are summarized in Table I.

TABLE I

	Ephedrine Added	Amount Unabsorbed	Alcohol Washing	Alcohol Washing
Dowex 50	0.2	0.105	0.060	0.002
Amberlite	0.2	0.043	....	....

Since only about one half the ephedrine was absorbed, one half the amount of alkaloid was used in the next experiment and 10 cc. portions of 95% alcohol were used in the washing of the resin. The results are given in Table II.

* Division of Pharmacy, Howard College, Birmingham, Ala.

TABLE II

	Ephedrine Added	Amount Unabsorbed	Alcohol Washing	Alcohol Washing
Dowex 50	0.1004	0.022	0.056	0.004
Amberlite IRC 50	0.1004	0.022	....	....

The experiment from which the data in Table II was obtained was repeated quantitatively and the exchangers were washed with hot alcohol. The results are given in Table III.

TABLE III

	Gm. Exchanger	Alkaloid Added	Amount Unabsorbed	Alcohol Washing	Alcohol Washing	Hot Alcohol	10 cc. n/10 HCl plus 10 cc. HOH
Dowex 50	6.11	0.1004	0.014	0.018	0.009	0.018	0.173
Amberlite IRC 50	6.30	0.1004	....	....	....	....	0.113

The results show that Dowex 50 combines with the hydrochloric acid. Amberlite IRC 50 shows some promise as an alkaloidal reagent. The fact that a little more ephedrine was found than was actually present is probably due to the fact that unneutralized alcohol was used in the washing of the resin. Alcohol was tried again as a solvent following the addition of hydrochloric acid. The results are reported in Table IV.

TABLE IV

	Gm. Exchanger	Alkaloid Added	Amount Unabsorbed	10 cc 0.1 HCl plus 10 cc Alcohol	Alcohol Washing	Diluted Alcohol Washing
Dowex 50 A	5.86	0.1004	0.027	0.052	0.003	....
Dowex 50 B	5.99	0.1004	0.022	0.053	....	....
Amberlite IRC 50	5.60	0.1004	0.005	....	....	....
Amberlite IRC 50	5.14	0.1004	0.004	....	....	....

This experiment shows that washing with alcohol and diluted alcohol after treatment with 0.1 N HCl is useless and these results are to be expected because ephedrine hydrochloride dissolves in 3 cc. water and about 14 cc. of alcohol (3). Water should be a better solvent.

Since the experiment repeated in Table III showed some possibilities it was repeated omitting the washings with alcohol but using water as a solvent. The results are reported in Table V.

TABLE V

	Gm. Exchanger	Column Height in Cm.	Ephedrine Added	Amount Unabsorbed	10 cc 0.1 HCl plus 10 cc. HOH
Dowex 50	7.92	7	0.1004	0.024	0.225
Dowex 50	9.60	6	0.1004	0.023	0.228
Amberlite IRC 50	7.45	6.5	0.1004	0.0003	0.112
Amberlite IRC 50	6.38	6.5	0.1004	0.0002	0.114

These results show that the Dowex 50 reacts with the O.1 N HCl since more alkaloid was found than was added. In the case of the Amberlite IRC 50, results indicate that the 0.1 HCl might be reacting with the amberlite. Another experiment was undertaken with just the Amberlite IRC 50 and the results are reported in Table VI.

TABLE VI

Gm. Amberlite IRC 50	Height of Column in Cm.	10 cc 0.1 N HCl plus HOH
5.81	8	0.003
5.46	6	9.004
5.59	6	0.004
7.59	6.5	0.003

These results show that of the 13 mg. excess of ephedrine obtained only 3 mg. can be accounted for by absorption of the hydrochloric acid.

Discussion.

The results indicate that Amberlite IRC 50 is a good absorbing media for a weak base such as ephedrine. This base is absorbed readily from an alcoholic solution. A solvent such as alcohol will not recover the alkaloid from the absorbing media but a solvent such as O.1 N hydrochloric acid combines with the base and regenerates the resin. The ion exchange reaction can be expressed by the following equation.

Resin alkaloid plus HCl yields Resin H plus Alkaloid Chloride. Since the reaction is reversible, the resin is regenerated and may be used again.

Summary.

1. The absorption and liberation of ephedrine from two ion exchange resins has been studied.

2. Amberlite IRC 50 has possibilities as an absorbent of ephedrine while Dowex 50 is unsatisfactory for absorption of ephedrine base.

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OFFICIAL PHARMACOPEIAS AND FORMULARIES IN USE IN THE DIFFERENT COUNTRIES OF AMERICA *

By Ricardo Galbis, Phar. D.

Country	National Pharmacopoeia	Adopted Pharmacopoeia
Argentina	Farmacopea Argentina, Tercera Edición, 1943.	
Bolivia		French
Brasil	Pharmacopeia dos Estados Unidos do Brasil, 1926.	
Canada	British Pharmacopoeia.	
Colombia		U.S.P., French & British
Costa Rica		U.S.P.
Cuba		U.S.P.
Chile	Farmacopea Chilena, Tercera Edición, 1941.	
Ecuador		French
El Salvador		French
Guatemala		French
Haiti		French
Honduras		U.S.P.
Jamaica	British Pharmacopoeia.	
México	Farmacopea Nacional de los EE. UU. Mexicanos.	
Nicaragua		U.S.P., & French
Panamá		U.S.P.
Paraguay	Farmacopea Paraguaya, 1945.	

* Reprinted through the courtesy of Asociacion Farmaceutica Nacional, Habana, Cuba.

Country	National Pharmacopoeia	Adopted Pharmacopoeia
Perú		French
Puerto Rico	U.S.P.	
Rep. Dominicana		French
United States of America	Pharmacopeia United States of America.	
Uruguay		French
Venezuela	Farmacopea de los EE. UU. Venezuela, la. edic. 1942.	

Out of the twenty-one American republics only seven possess their own pharmacopoeia: Argentina, Brasil, Chile, México, Paraguay, United States of America and Venezuela.

Bolivia, El Salvador, Guatemala, Haití, Perú, República Dominicana and Uruguay have adopted the French pharmacopoeia.

Costa Rica, Cuba, Honduras and Panamá have adopted the U.S.P.

Colombia, Ecuador and Nicaragua have adopted both the French and the U.S.P.

Possesions, of course, use the pharmacopoeia of the ruling power.

Only four nations have their own national formulary: Canada, Cuba, Paraguay and the United States of America. With the advent of the International Pharmacopoeia it is logical that those countries having no national pharmacopoeia will adopt this international standard, or this international Pharmacopoeia will serve as a nucleus to form their national pharmacopoeias.

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SELECTED ABSTRACTS

Vitamin B_{12} and Folic Acid in Megaloblastic Anemias of Pregnancy and the Puerperium. C. C. Ungley and R. B. Thompson. *Brit. Med. J. No. 4659*:919 (1950). Megaloblastic anemia of pregnancy and the puerperium is distinct from Addisonian pernicious anemia with its associated gastric atrophy and the permanent loss of Castle's intrinsic factor. In this series of six patients the hematological picture included megaloblastic bone marrow in each case. In five of the cases 80 micrograms of vitamin B_{12} and in one case 65 micrograms of the vitamin were given intramuscularly. However, there was no response and the rapid destruction of blood cells transfused into the body continued. This dose was many times that required to produce a prompt response in Addisonian pernicious anemia. The serious state of the patients prompted the administration of folic acid. In every case there was a marked response. The dose in 3 of the patients was only 2.5 mg. of folic acid a day. In two of the patients this dose was given orally and intramuscularly on alternate days. In one patient 30 mg. was given intravenously and in 2 patients 20 mg. was given by mouth. Within a few days there was a marked change in the blood picture of each patient: excessive hemolysis ceased, the rate of elimination of transfused blood fell to normal, the patients' own red blood cell count increased, and the bone marrow returned to normal.

The authors pointed out that the patients gave a history of a rather normal diet with no indication that the intake of foods containing folic acid was lower than in other pregnant women of similar social status who did not develop megaloblastic anemia.

Vitamin B_{12} in Macrocytic Anemia of Pregnancy. J. C. Patel and B. R. Kocher. *Brit. Med. J. No. 4659*:924 (1950). Proof has been given of the effectiveness of vitamin B_{12} in the treatment of Addisonian pernicious anemia, nutritional macrocytic anemia, and in

tropical macrocytic anemia. However, the results have not been encouraging in cases of macrocytic anemia of pregnancy.

As a result of the treatment of the five cases reported by the authors the conclusion was reached that insufficient medication had been given in previous trials. It appears that 4 micrograms a day or more are required to produce optimum results in the treatment of macrocytic anemia of pregnancy as compared with 1 microgram a day in the treatment of Addisonian pernicious anemia.

In 4 of the 5 cases in this series 40 micrograms of the vitamin were given in a single intramuscular injection and then the patients were observed for 14 days. The fifth case received 20 micrograms. Improvement was prompt in every case and in 3 cases the response was optimum. The fifth case experienced a partial and temporary response, and when a 40 microgram dose (divided) was given to this patient the response was suboptimum. The suboptimum response was judged on the basis of the reticulocyte response and by the increase in red blood cells and hemoglobin. The first case discussed also experienced a suboptimum response with 40 micrograms. This effect was judged by the hemopoietic response and particularly the failure of the bone marrow to become completely normoblastic. In 3 of the cases there was also observed a maximum effect by the tenth day following the administration of the vitamin with a decline by about the 18th day. The authors therefore concluded that 40 micrograms or more of vitamin B_{12} are required to produce an optimum response during a period of 10 days. In one case 3 injections of 40 micrograms at 14 day intervals raised the number of red blood cells from 880,000 to 3,720,000 per c.mm. over a period of 44 days.

The Combined Action of Penicillin With Streptomycin or Chloromycetin on Enterococci In Vitro. E. Jawetz, J. B. Gunnison, and V. B. Coleman. *Science 111*:254 (1950). Previous studies have shown a synergism of action between penicillin and streptomycin against certain staphylococci and streptococci. It has also been shown that penicillin and streptomycin combined have been effective in the control of bacterial endocarditis caused by enterococci when ordinarily neither antibiotic could be expected to control the infection alone. This study was designed to test further the apparent synergism of

these two antibiotics against enterococci. Chloromycetin was also included in the study since it appeared that Chloromycetin interfered with the action of penicillin on many strains of enterococci *in vitro*.

The results obtained with 9 strains of enterococci were fairly uniform. The optimal concentration of crystalline sodium penicillin G was found to be 6 micrograms per cc. of culture media. With this concentration there was a rapid decrease in the count of viable bacteria to a low in 48 hours but after this there was a rise again until the count remained slightly below the count in the control tubes for at least 10 days. When concentrations of penicillin as high as 300 μg/cc. were used the decrease in viable bacteria occurred much more slowly and not all bacteria were killed in 7 to 10 days, but after prolonged incubation all of the bacteria were killed in some tubes.

Concentrations of 25 to 50 μg/cc. of streptomycin sulfate completely failed to inhibit the growth of the bacteria in the inoculum. However, when 25 μg/cc. of streptomycin was added to 6 μg/cc. of penicillin the rate of bactericidal action was greater than with penicillin alone and within 3 to 5 days there was complete sterilization of the medium. The fact that the bactericidal action of penicillin was at an optimum and could not be increased by either an increase or a decrease in concentration and since streptomycin alone was completely ineffective the action of the combined antibiotics must be true synergism. The rapid rate of death of the entire enterococcal population indicates at least a tenfold potentiation of penicillin action.

To test the possibility that the greater effectiveness of the combined action over either antibiotic alone might be the result of an inhibition of the development of penicillin-resistant strains, sensitivity tests were performed after the organisms had been exposed to penicillin alone. There was no indication that these organisms had developed increased penicillin resistance and they were no more susceptible to streptomycin.

Chloromycetin alone in a concentration of 10 μg/cc. had no significant effect on the bacterial population, but when combined with the optimum concentration of penicillin there was a pronounced effect. The rate of bactericidal action was less than with penicillin alone for the low count of viable bacteria reached by penicillin alone in 24 hours was not reached by the combination until the 6th to 12th day. Therefore, Chloromycetin appears to have some sort of antagonistic

action to that of penicillin. However, whereas penicillin alone permitted an increase of viable bacteria after the low had been reached the combination of penicillin and Chloromycetin behaved similar to the 300 μg/cc. concentrations of penicillin in that the bactericidal action was much slower but eventually in some of the tubes all of the enterococci succumbed.

Thus it would seem to be a demonstrable fact that penicillin-streptomycin synergism on enterococci increases the rate of bactericidal action beyond the optimum obtainable with penicillin alone.

Relationship of In Vitro Tests of Antifungal Substances to Therapeutic Problems. K. A. Oster and M. J. Golden. *Trans. N. Y. Acad. Sci. 12*:132 (1950). The authors challenge the almost uniformly expressed opinion in textbooks that dermatophytosis should not be treated with strong fungicides. Their article seeks to prove that this traditional statement is not valid.

Since the primary concept for the treatment of any infectious disease is the employment of proper chemotherapy, the treatment of a dermatophytosis should be the employment of a fungicidal agent. The authors point out that previous experiments with 10 of the most frequently used antifungal substances revealed that none of them were fungicidal in the concentrations normally employed. The test employed was one developed by the authors and is a manifestation of the relationship between a controlled contact time of fungus and toxicant, established by a washing step, and the concentration of the drug. It was pointed out that the trichophytons grow on dead and macerated skin exclusively and therefore the cure of such an infection is not dependent upon the body's own defense mechanisms in any way but is solely dependent upon the effectiveness of the chemotherapeutic agent. Therefore, a proper fungicidal test should provide the answer to the correct concentration of the chemical to be used in actual therapy.

A very limited study was also made by the authors regarding the development of resistance to fungistatic agents by fungi. They found that after growth for a period of one week in dilutions of undecylenic acid and of hydroxyquinoline, increased amounts of these substances were required to produce stasis.

The authors then proceed to discuss the course of healing of a tinea pedis infection. They suggested that the very high incidence of recurrences of this type of infection are the result of the use of antifungal substances that are too weak to eradicate the infection completely. The parasite would then lie quiescent until favorable conditions for growth were again present. Provided the antifungal agent was not a primary irritant there would be little or no irritation of the host's tissue. However, they suggested that quite a different healing process would be encountered if a truly fungicidal substance were employed. The inherent effectiveness of the fungicidal substance would activate the dormant sites of infection and there would be an apparent spread of the infection or, it might appear that there was a primary irritation from the fungicide itself. After this initial spreading the fungicide would completely eradicate the infection. This spreading would be the result of the activation of quiescent foci of infection by the toxins from killed fungi.

The authors contend that although the sudden release of fungus toxins may precipitate a trichophytid reaction, such a reaction should not be sufficiently severe to be an obstacle to the use of powerful fungicidal agents in the treatment of dermatophytoses.

BOOK REVIEWS

Organic Chemistry in Pharmacy. Edited by Charles O. Wilson and Ole Gisvold with Troy C. Daniels, W. D. Kumler, Eldin V. Lynn, Taito O. Soine, Abraham Taub, and Heber W. Youngken, Jr., as collaborating authors; 622 pages incl. index. J. B. Lippincott Co., Philadelphia, London, Montreal. Price $9.00.

This is an entirely new book developed to provide a suitable text for the teaching of the pharmacy and chemistry of organic medicinals. Following a brief introductory chapter is a chapter titled "Physical Properties in Relation to Biologic Action" and another titled "Metabolic Changes of Drugs and Related Organic Compounds in the Body (Detoxication)." The remainder of the text is arranged following the usual system employed in organic chemistry with the aliphatic compounds followed by the aromatic compounds and heterocyclics. Special chapters on "Compounds Containing Metals", "Surface Active Agents", "Glycosides", "Steroids", "Plant Alkaloids", "Antibiotics", "Vitamins", "Proteins and Amino Acids" and "Botanical Oleoresins, Resins and Balsams" are also included.

The authors are to be complimented for having accomplished such a fine balance between the theoretical and the practical. The material presented is quite up to date and good judgment is evident in the selection of data and information for inclusion. Although some of the subject matter is likely to be beyond the average undergraduate student, it is so skillfully incorporated that the average student will not get "mental indigestion". Its presence will serve as a stimulus to the above average student and give him a thorough background should he wish later to continue into graduate work.

Those who are engaged in teaching will find this book of great value in the preparation of their courses. The authors have rendered a service to pharmaceutical education in the difficult task of preparing this entirely new book and it is probably the best representative of the several newly developed texts introduced in the field of pharmacy in the last five years.

L. F. Tice

Inorganic Chemistry in Pharmacy. By Lloyd M. Parks, Paul J. Jannke, Loyd E. Harris and John E. Christian; 298 pages incl. index. J. B. Lippincott Co., Philadelphia, London, Montreal. Price $6.00.

This is a new textbook intended for use in courses of inorganic pharmaceutical chemistry as given to pharmacy students. The method chosen by the authors in the presentation of the subject is in agreement with the more modern concepts of inorganic chemistry. Compounds are classified and presented as hydrides of the elements, metallic compounds of the elements or metallic substitution products of the hydrides, hydroxides of the elements and salts of the oxyacids or metallic substitution products of the hydroxides.

The authors have done an excellent job in preparing this text and the publishers are to be complimented on the fine format and appearance of the book. It would appear, however, from an examination of the text that the educational level is somewhat beyond what may be expected of undergraduate students majoring in pharmacy. It is indeed an excellent goal for achievement but few pharmacy majors whose objective is retail pharmacy are likely to master its difficulties. Students who are preparing for graduate work will find this text excellent and a thorough presentation of material which every graduate student should possess. The authors, who are recognized experts in the field of graduate education in pharmacy, have possibly over-estimated the capacity of the average pharmacy undergraduate studying today in our crowded four year curriculum.

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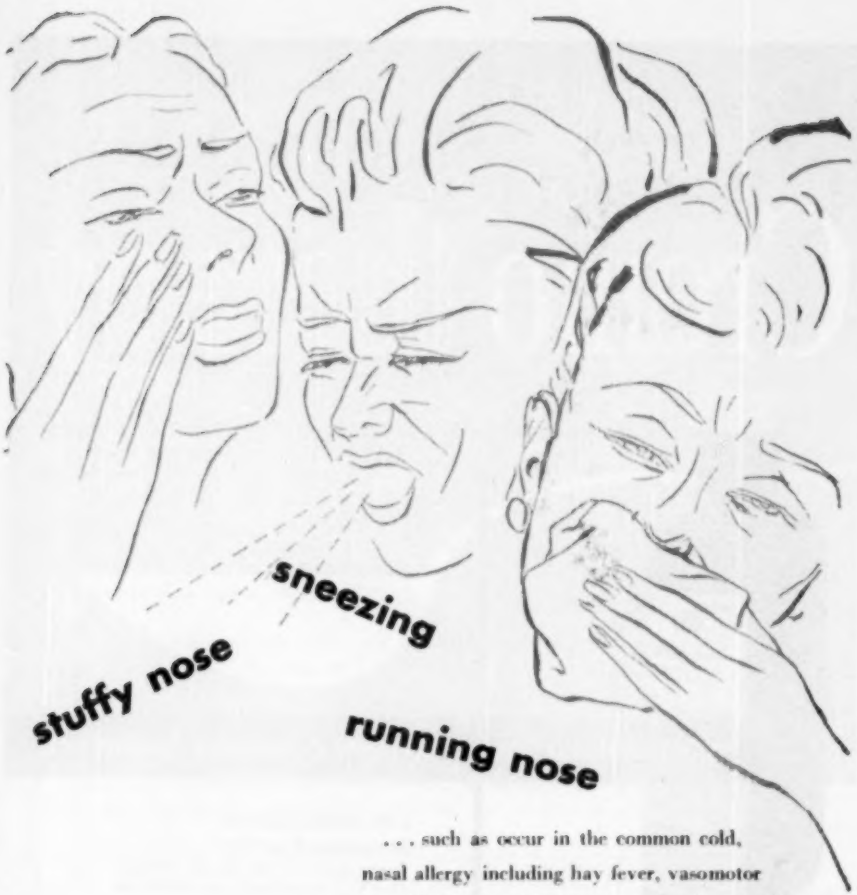

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